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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/450,217	11/29/1999	PETER ERDMANN	8265-296-999	7310

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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1653	19

DATE MAILED: 02/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/450,217	ERDMANN ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-19 and 21-26* is/are pending in the application.

4a) Of the above claim(s) *14-19 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-13 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Pursuant to the directives of paper No. 18 (filed 11/12/02), claims 5 and 20 have been cancelled, claims 1, 4, 6, 12, 19 amended, and claims 24-26 added. Claims 1-4, 6-19, 21-26 remain pending.

Claims 14-19 and 21-23 remain withdrawn from consideration. Claims 1-4, 6-13, 24-26 are examined in this Office action.

Applicants' arguments filed 11/12/02 have been considered and found persuasive in part. However, the §103 rejections are maintained.

*

Claims 1-4, 6-13, 24-26 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 1 is drawn to a process for obtaining a "fraction" which contains GMP. This term "fraction" is viewed as primarily encompassing mixtures (although pure GMP is not necessarily precluded as one possible embodiment). A mixture, however, must contain at least two components. If a mixture consists of a pure compound, it is not a mixture. Accordingly, the claims mandate the presence of a compound or compounds in addition to the GMP. Is the second component another whey protein, is it water, or is it something else? The claims are silent as to what this second component might be. As such, the claims are rendered indefinite. It is suggested that the claims be amended to recite either of the following: (a) that the pure GMP is isolated, or (b) that a mixture is obtained which contains GMP in addition to a specified second compound.

- Claim 8 recites the phrase "between about 4.5 to 5.5", thus rendering the claim indefinite as to the upper and lower limits of pH.

- In claim 12, the phrases "the eluate" and "the washings" both lack antecedent basis.

- Claim 12 requires that GMP be "desorbed". However, there is no suggestion in either claim 1 or claim 12 that GMP must be absorbed (or adsorbed) in the first place. Accordingly, a key process step is missing from either claim 1 or claim 12.

- Claim 26 is a substantial duplicate of claim 25. In traversing, applicants are requested to explain, in physical terms, what exactly the difference is between the composition of claim 25, and that of claim 26. Alternatively, it is suggested that claim 26 be cancelled.

*

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1-4, 8-13, 24-25 are rejected under 35 U.S.C. §103 as being unpatentable over Shimatani (USP 5,434,250).

As indicated previously, Shimatani teaches (beginning at col 2, line 67) a process of obtaining GMP by passing desalted whey, at acidic pH, through a cation exchanger.

Additionally, claim 5 of the patent (col 6, line 23+) teaches a process of obtaining GMP by passing whey, at acidic pH, through a cation exchanger, and then employing the further step of ultrafiltration.

Applicants have traversed by arguing that the reference teaches a process for obtaining sialic acids, rather than GMP. However, applicants are not correct. While it may be true that the reference suggests that one of the embodiments of the invention might be recovering a sialic acid, the fact remains that the reference does teach a method of obtaining a composition comprising GMP (see e.g., col 2, line 65) or pure GMP (e.g., col 6, line 33+). Applicants have also argued that Shimatani does not teach the step of removing GMP from the deionized lactic raw material by contacting the lactic raw material from with a cation exchanger.

The first point is that the "lactic raw material" can be just about any mixture that contains, or previously contained GMP. Of course, the mixture would be primarily limited to proteins, sugars, and fats that are normally found in dairy products. Such proteins include the following: *alpha*-, *beta*-, *gamma*- and *kappa*-caseins, *alpha*-lactoglobulin, *beta*-lactoglobulin, iron-binding proteins, lactollin, albumin, acid phosphatase, amylase, lipase, lysozyme, ribonuclease, and immunoglobulins. See, for example, McKenzie (*Advances in Protein Chemistry* **22**, 55-234, 1967). Thus, a "lactic raw material" could be e.g., a mixture of GMP in combination with *alpha*-casein, albumin, and lactollin. Or a "lactic

raw material" could be e.g., a mixture of GMP in combination with albumin, IgG, and *alpha*-lactoglobulin. The possibilities are endless. As it happens, Shimatani teaches that if whey is applied to a cation exchanger, *beta*-lactoglobulin binds (to the column) to a greater extent than *alpha*-lactoglobulin or GMP, and that in this way, a separation is achieved between *beta*-lactoglobulin (on the one hand) and *alpha*-lactoglobulin and GMP (on the other hand). Given the absence of any limitations on the meaning of the term "lactic raw material", the fact is that the fraction (of Shimatani) which is enriched in *beta*-lactoglobulin could be a "lactic raw material"; similarly, the fraction which is enriched in *alpha*-lactoglobulin and GMP could also be a "lactic raw material". Alternatively, the fraction which is enriched in *alpha*-lactoglobulin and GMP could be a "GMP enriched fraction". The point is that the claims do not mandate that any one (or more than one) specific protein be separated from the GMP; all that matters is that the concentration of GMP in the final mixture is somewhat higher than that which was present in the initial mixture. Setting aside for a moment the specifics of the claims, suppose that one had 100 mL of a "lactic raw material", and that it contained 50 mg of *alpha*-lactoglobulin, 50 mg of GMP and 50 mg of *beta*-lactoglobulin, along with various amounts of *alpha*-, *beta*-, and *gamma*-caseins, iron-binding proteins, lactollin, albumin, acid phosphatase, amylase, lipase, lysozyme, ribonuclease, and immunoglobulins. Call it the "first LRM". In this example, water is by far the most abundant component of the "first LRM". Suppose that one were

to remove, e.g., 10 mL of water from the "first LRM", thereby generating 90 mL of a "second LRM". The fact is that the "second LRM" would be "enriched" in GMP relative to the "first LRM"; in the "first LRM", GMP is present to the extent of only 500 mg/liter, but in the "second LRM", GMP is present to the extent of 556 mg/liter. Or suppose that one had a "third LRM" which is obtained by lyophilizing a given lactic raw material, and suppose further that in this "third LRM", albumin constitutes e.g., 50% by weight, and GMP just 3% by weight. If one could achieve the objective of removing all of the albumin (generating a "fourth LRM"), leaving the other proteins intact, the result would be that the concentration of GMP in this "fourth LRM" would be 6% of the total weight, as opposed to just 3% in the "third LRM". Thus, the "fourth LRM" would then be "enriched" in GMP, at least relative to the "third LRM". This analysis using the first, second, third, and fourth "LRM" does not address all of the issues of the claims, but it makes an important point, which is that obtaining a "fraction" which is "enriched" in GMP is a very modest limitation, which can be achieved by removing virtually any of the initial components of the "lactic raw material".

In view of the foregoing, it should be clear that Shimatani discloses a method of obtaining a fraction in which the relative amount of GMP is greater than it was in the initial "lactic raw material" (see e.g., col 2, line 65 or col 6, line 33+). Applicants have also argued that the following limitation is not taught by the reference:

> "separating the anionic resin having absorbed GMP from the treated liquid material followed by separating the GMP fraction from the resin".

As it happens, however, the phrase recited by applicants does not appear in the claims. First, there is no requirement in the claims that one ever have a resin to which GMP is absorbed. But even if there were such a requirement, a chromatographic specialist of ordinary skill would have expected that some adsorption of GMP would have occurred. This is because while GMP will have a net negative charge above its IEP (isoelectric point), and a net positive charge below its IEP, at a pH range of 2-4 the GMP will have many positively charged amino acid side chains. Accordingly, one would not expect GMP to elute in the "void volume", but that it would be retained to a small degree by the anionic groups of the resin. In any case, however, the question of GMP eluting "in" the void volume versus *after* the void volume is moot insofar as the presently rendered claims are concerned. As it happens, the reference most certainly does teach "separating the anionic resin" from the GMP, regardless of the degree of adsorption which may have occurred. Any time a chemist elutes a mixture of proteins from a column, be it ion exchange, affinity chromatography, size exclusion chromatography, or hydrophobic ineraction chromatography, one is "separating" the proteins (at least those that have eluted) from the resin. Consider again what applicants have argued that the reference fails to render obvious:

> "separating the anionic resin having absorbed GMP from the treated liquid material followed by separating the GMP fraction from the resin".

As it happens, the phrase "followed by" does not appear in the claims. The claims do not specify any particular order of the process steps. The claims do not require that the GMP enriched fraction be separated from the resin after the resin has been separated from the "treated liquid material"; the claims permit the GMP enriched fraction to be separated from the resin before the resin is separated from the "treated liquid material"; and the claims permit the GMP enriched fraction be separated from the resin at the same time as the resin is being separated from the "treated liquid material".

Consider what is not being claimed:

100. A process for obtaining a fraction of a LRM (lactic raw material) enriched in GMP comprising:

> *(a) contacting a LRM with a cation exchange resin for a time and under conditions effective to adsorb GMP, wherein said LRM contains GMP and at least one additional whey protein;*
>
> *(b) eluting the cation exchange resin for a time and under conditions effective to produce an eluate containing said at least one additional whey protein, and wherein the GMP remains adsorbed to the cation exchange resin;*
>
> *(c) discarding the eluate of step (b);*
>
> *(d) eluting the cation exchange resin for a time and under conditions effective to remove GMP from said resin, thereby generating a fraction of LRM which is enriched in GMP.*

The foregoing is not necessarily a suggestion for claim language, but is provided as a contrast between what is claimed, and what is not being claimed. As it happens, this claim (claim

100) comes much closer to the *argued* limitations than does claim 1 as currently rendered.

Thus, Shimatani renders obvious a process in which all of the process steps of the claims are met.

*

Claims 1-4, 8-13, 24-25 are rejected under 35 U.S.C. §103 as being unpatentable over Shimatani (USP 5,434,250) in view of Marshall (*Food Research Quarterly* **51**, 1991, reference "AL" on the IDS).

The teachings of Shimatani and Marshall were indicated previously. Applicants have not specifically traversed this rejection, other than to suggest that Shimanti taken by itself is inadequate, and that therefore Shimatani in view of Marshall must be inadequate as well.

In response, the arguments presented above (Shimatani taken by itself) are incorporated by reference herein. The rejection is maintained.

*

Claims 1-4, 8-13, 24-25 are rejected under 35 U.S.C. §103 as being unpatentable over Kawasaki (USP 5278288)

Kawasaki discloses (col 2, line 62+) a process of preparing GMP by contacting milk raw materials with a cation exchanger. The recommended pH is in the range of 3-4.5 (col 3, line 62+) . Also, in example 1 (col 6, line 3+) a pH of 4.0 was usd in conjunction with an anionic resin. The reference suggests collecting a fraction which does not

adsorb on the anionic resin; however, this meets the limitations of the claims which require only "removal" of the GMP from the lactic raw material.

In response, applicants have argued that the instant claims mandate adsorption of the GMP onto the cation exchange resin. However, applicants are not correct. In maintaining this argument applicants are requested to be very specific in citing the passage from the claims which mandates this. Applicants have also argued that Kawasaki does not teach "removal" of the GMP from the lactic raw material. However, this is disclosed for example, at col 2, lines 59-61.

The rejection is maintained.

*

Claims 25-26 are rejected under 35 U.S.C. §103 as being unpatentable over Shimatani (USP 5,434,250) in view of Drouet (USP 5,063,203).

The teachings of Shimanti were indicated previously. Shimatani does not disclose that GMP inhibits thrombosis. Drouet discloses that GMP inhibits thrombosis, but does not disclose the claimed process.

Thus, it would have been obvious to one of ordinary skill at the time of the invention to combine the GMP with a pharmaceutically acceptable carrier in order to obtain a composition which inhibits thrombosis.

*

Claims 25-26 are rejected under 35 U.S.C. §103 as being unpatentable over Kawasaki (USP 5,278,288) in view of Drouet (USP 5,063,203).

The teachings of Kawasaki are indicated above. Kawasaki does not disclose that GMP inhibits thrombosis. Drouet discloses that GMP inhibits thrombosis, but does not disclose the claimed process.

Thus, it would have been obvious to one of ordinary skill at the time of the invention to combine the GMP with a pharmaceutically acceptable carrier in order to obtain a composition which inhibits thrombosis.

*

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1600